REMARKS

Claims 26-29, 33, 37 and 39 are pending in the application after entry of this amendment. Claims 33 and 39 are currently amended, and claims 35, 38 and 40 are cancelled, without prejudice to or disclaimer of any previously presented subject matter. Claim 39 stands withdrawn from consideration. No new matter has been added.

Applicants note that claims 33, 35 and 38-40, which were cancelled in the Examiner's Amendment dated May 29, 2009, have been re-instated by the Examiner in the present Office Action. As noted above, claims 35, 38 and 40 are cancelled with this amendment.

Claim 33 has been amended to remove the solvent diethylene monobutyl ether and to remove the phrase "and the like." Dependent claim 39 has been amended to recite the formula of the thioamide derivative of fipronil. No new matter has been added.

Applicants respectfully request reconsideration of the amended claims. Further, Applicants respectfully request withdrawal of the claim rejections identified in the Office Action of record dated October 2, 2009 in view of the amendments and remarks herein.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 33 is rejected under 35 U.S.C. § 112 second paragraph as allegedly indefinite. The Examiner asserts that the phrase "and the like," renders the claim indefinite. Claim 33 has been amended to remove the phrase from the claim. Accordingly, Applicants respectfully request withdrawal of the rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claim 33 is rejected under 35 U.S.C. § 112 first paragraph as not enabled by the specification. The Examiner asserts that although the specification is enabling for a premix comprising a compound of formula (II) and i) a pharmaceutically acceptable wax, ii) a pharmaceutically acceptable antioxidant, and iii) a pharmaceutically acceptable carrier as recited in claim 33, the specification does not reasonably provide enablement for a premix containing an organic solvent, with the exception of propylene glycol. The Examiner asserts that the solvents recited in claim 33 are typically used dermally, and that there is no disclosure in the specification

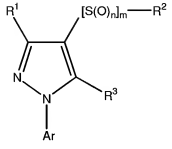
as to how much solvent to use. The Examiner further asserts that the examples are free of these solvents.

Contrary to the Examiner's assertion, the specification contains two examples that describe premixes that include the solvents recited in the claim. For example, Examples 7 and 8 on page 86 of the specification describes a premix that includes propylene glycol in an amount of 0.35 % and 15% (w/w), respectively. Example 10 on page 87 of the specification describes a premix that contains the solvent diethylene glycol monobutyl ether in an amount of 10% (w/w). In addition to propylene glycol and diethylene glycol monobutyl ether, claim 33 recites the solvents diethylene glycol monoethyl ether and diethylene monobutyl ether. Solely to expedite allowance of the application, claim 33 has been amended to remove the solvent diethylene monobutyl ether. The solvent diethylene glycol monoethyl ether is a common solvent used in pharamaceutical and veterinary compositions and is known as Transcutol®. This solvent is in the same class as diethylene glycol monobutyl ether and has a very similar structure. Use of diethylene glycol monoethyl ether in the premixes of the invention is explicitly described on page 20, paragraph 3, of the specification. Based on the description in the specification, including the specific formulation of Example 10 which includes the very closely related solvent diethylene glycol monobutyl ether in a specific amount, Applicants respectfully submit that the specification provides sufficient guidance for one of skill in the art to make and use the premix of claim 33. Accordingly, claim 33 is fully enabled by the specification and the state of the art. Withdrawal of the rejection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 26-29, 33 and 37 stand rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 6,518,296 to Alig *et al.* (Alig) in view of U.S. 2004/0037869 to Cleverly *et al.* (Cleverly), U.S. Patent No. 6,569,886 to Huber *et al.* (Huber) and U.S. 2005/0136087 to Freehauf *et al.* (Freehauf). The Office Action asserts that Alig shows the compounds recited in the claims in example 4 of Table 1A, and that it would have been obvious for one of ordinary skill in the art at the time the invention was made to attain the premixes recited in the claims based on the teaching of Alig in view of Cleverly, Huber and Freehauf. Applicants respectfully disagree and request reconsideration of the amended claims in view of the comments below.

Contrary to the Examiner's assertion, Alig does not show the compound recited in the claims or suggest such compounds. Alig relates to 3-thiocarbamoylpyrazole compounds of formula (I) below, where variable R^1 at the 3-position of the compound is the group H^2N-C(=S)-, and the group at the 4-position of the pyrazole ring is $-[S(O)_n]_m-R^2$, where n is 0, 1 or 2, and m is 0 or 1.



(I)

The $[S(O)_n]_m-R^2$ group at the 4-position of the pyrazole ring requires that when m is 1 the group R^2 is directly bonded to the sulfur atom. The groups R^2 may be various functional groups (see column 1, line 30 to column 2, line 9) but not haloalkyl, haloalkenyl or haloalkynyl.

In contrast, the thioamide arylpyrazole derivatives recited in claims 26 and 33 contain the groups $-S(O)_nR^3$ or 4,5-dicyanoimidazol-2-yl at the 5-position of the pyrazole ring, where R^3 is haloalkyl, haloalkenyl or haloalkynyl. The group 4,5-dicianoimidazol-2-yl is not mentioned or suggested by Alig. Further, Alig does not permit compounds that include the group $-S(O)_nR^3$ at the 5-position of the pyrazole ring where R^3 is haloalkyl, haloalkenyl or haloalkynyl.

In the Office Action of record dated December 11, 2008, the Examiner asserted that the groups $-CH_2S(O)CF_3$, $-CH_2C(O)OCF_3$, $-CH_2SCH_2CH_2-O-CH_2CF_3$ and $-CH_2-SCF_3$ in the definition of R^2 of Table 1 of Alig provided for haloalkyl groups. Applicants respectfully submit that these groups are not haloalkyl groups but various functional groups that contain a haloalkyl component. It would be clear to one of skill in the art that these groups would be named "haloalkylsulphinylalkyl," "haloalkoxycarbonylalkyl," "haloalkoxyalkylthioalkyl," and "haloalkylthioalkyl" groups, respectively. This is consistent with the functional groups "halogenoalkylsulphinylalkyl," (col. 1, line 35) "halogenoalkoxycarbonylalkyl," (col. 1, line 40) "halogenoalkoxyalkylthioalkyl,"(col. 1, line 45) and "halogenoalkylthioalkyl"(col. 1, line 35) which are explicitly described for the definition of R^2 in Alig. In contrast, a simple haloalkyl group would be clear to one of skill in the art as an alkyl group in which one or more of the

hydrogen atoms is replaced by a halogen atom and would not include a heteroatom, a sulfinyl group or an ester group, just as a simple alkyl group would not include these groups within the chain.

Alig describes that R^2 may include certain haloalkyl-containing functional groups, but these functional groups do not allow a haloalkyl to be directly bond to the sulfur of the $[S(O)_n]_m$ group. The haloalkyl-containing groups in the definition of R^2 of Alig are "halogenoalkylthioalkyl," "halogenoalkylsulphinylalkyl," "halogenoalkylsulphonylalkyl," "halogenoalkoxycarbonylalkyl," "halogenoalkoxycarbonyl," "halogenoalkoxyalkyl," "halogenoalkoxyalkylthioalkyl," "halogenoalkoxyalkylsulphinylalkyl," and "halogenoalkoxyalkylsulphonylalkyl" (see column 1, line 30 to column 2, line 9 of Alig). All of these groups require a heteroatom-containing functional group and a diradical alkylene group between the haloalkyl group and the $[S(O)_n]_m$ group, rendering the compounds of Alig significantly different than the compounds recited in the claims.

For example, the group "halogenoalkylthioalkyl" includes a sulfur atom and a diradical alkylene group between the halogenoalkyl (haloalkyl) group and the $[S(O)_n]_m$ group (e.g. haloalkyl-S-$(CH_2)_n$-), and the group "halogenoalkylsulphinylalkyl," contains a sulphinyl group (-S(O)-) and a diradical alkylene group between the haloalkyl group and the $[S(O)_n]_m$ group. Similarly, the groups "halogenoalkylsulphonylalkyl," "halogenoalkoxycarbonylalkyl," "halogenoalkoxycarbonyl," "halogenoalkoxyalkyl," "halogenoalkoxyalkylthioalkyl," "halogenoalkoxyalkylsulphinylalkyl," and "halogenoalkoxyalkylsulphonylalkyl" contain the groups [-$S(O)_2$-alkylene-], [-O-C(O)-alkylene-], [-O-C(O)-], [-O-alkylene-], [-O- alkylene-S-alkylene-], [-O-alkylene-S(O) -alkylene-] and [-O-alkylene-$S(O)_2$-alkylene-], respectively, between the haloalkyl radicals and the $[S(O)_n]_m$ group that is bonded to the 4-position of the pyrazole ring of the compounds. In contrast, the compounds recited in the claims require that the 4-position of the pyrazole ring have a -$S(O)_n$-haloalkyl, -$S(O)_n$-haloalkenyl or -$S(O)_n$-haloalkynyl group, in which the haloalkyl, haloalkenyl or haloalkynyl group is directly bonded to the -$S(O)_n$ group.

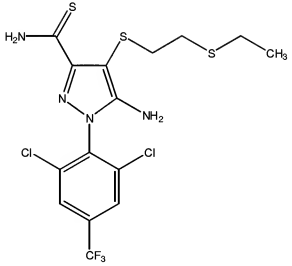
Furthermore, non of the compounds shown in Table 1 of Alig (see column 10, line 40 to column 11), include a substituent with a haloalkyl group in the definition of R^2. Consistent with the description in column 1, line 30 to column 2, line 9 of Alig discussed above, all of the haloalkyl-containing groups in the definition of R^2 in Table 1 include a heteroatom and an

alkylene group between the haloalkyl and the sulfur atom of the group $[S(O)_n]_m$. For example, the groups $-CH_2-SCF_3$, $-CH_2-SO-CF_3$, $-CH_2-CO-OCF_3$, $-CH_2-S-CH_2CH_2-OCH_2CF_3$ in the definition of R^2 in Table 1 do not allow a haloalkyl group to be direct bonded to the $[S(O)_n]_m$ group.

Similarly, non of the compounds in Table 13 of Alig include a haloalkyl group directly bonded to the $[S(O)_n]_m$ group, as required in the claims. The only haloalkyl-containing group, $-CH_2-SCF_3$, in the definition of R^2 in Table 13 requires a sulfur and $-CH_2-$ between the CF_3 group and the $[S(O)_n]_m$ group.

Table 14 in column 17 of Alig shows compounds that do not have a $-S(O)_n$ group at the 4-position of the pyrazole ring. These compounds require that the R^2 group is directly bonded to the pyrazole ring, and are significantly different than the compounds recited in the claims. For example, the haloalkyl groups $-CF_3$, $-OCF_3$ and $-CH(OH)CF_3$ in the definition of R^2 must be directly bonded to the pyrazole ring, not to a $-S(O)_n$ group, as required in the pending claims.

Further, contrary to the Examiner's assertion, Alig does not describe or suggest the thioamide derivative of fipronil. Example 4 in Table A of Alig (see columns 33 and 34) is not the thioamide derivative of fipronil. The structure of example 4 of Alig, which is shown below, has a alkylthioalkylthio group at the 4-position of the pyrazole ring. In contrast, the thioamide derivative of fipronil requires a trifluoroalkylsulphinyl group ($-S(O)-CF_3$) at this position.



In summary, Alig does not describe or suggest the compounds recited in the claims, which require that the 4-position of the pyrazole ring be substituted with a $-S(O)_n$-haloalkyl, $-S(O)_n$-haloalkenyl or $-S(O)_n$-haloalkynyl group. Alig does not describe or suggest that the 3-

thioamide-substituted compounds are converted to the corresponding compounds having a cyano group at the 3-position of the pyrazole ring or that administration of the 3-thioamide substituted compounds topically or orally provides the corresponding 3-cyano substituted compound in concentrations that are therapeutically significant. This is particularly useful with the thioamide of fipronil, which is not described or suggested by Alig.

The compounds of the invention, which have a different substitution pattern than the compounds of Alig would be expected to impart unique properties to the compounds, and the impact of such properties with respect to effects on biological properties is not obvious. It is well accepted in the art that the effect of structural modifications in biologically active molecules is not predictable. Accordingly, the compounds recited in the claims which are not described or suggested by Alig can not be considered obvious as Alig provides no information on the impact such changes on the biological activity or toxicology of the compounds. On the contrary, based on Alig, one of skill in the art would not expect that compounds having a $-S(O)_n$-haloalkyl, $-S(O)_n$-haloalkenyl or a $-S(O)_n$-haloalkynyl group at the 3-position of the molecule would result in favorable biological properties because these compounds are excluded from the extremely large number of possible compounds encompassed by the formula (I) of Alig. In the absence of any suggestion or motivation to modify the compounds of Alig to produce the compounds recited in the claims, the premixes in the claims cannot be considered obvious in view of Alig.

Cleverly describes chewable veterinary formulations or tablet formulations that may comprise a variety of active agents in combination with a filler, a disintegrant, a non-animal containing flavor, a binder, a humectant and a granulating solvent. Cleverly describes that the chewable or tablet formulations may include a variety of active agents, including fipronil and certain other arylpyrazoles that contain a cyano group at the 3-position of the pyrazole ring. However, Cleverly does not describe or suggest any formulations that include an arylpyrazole thioamide derivatives or provide any motivation to produce premix compositions containing any thioamide derivatives of arylpyrazole compounds.

Huber describes methods for controlling parasites in or on animals, which comprise administering certain non-emetic arylpyrazole compounds having oxygen-linked substituents at the 5-position of the pyrazole ring orally to the animal. The compounds described in Huber are distinct from the compounds recited in the claims. For example, although the compounds described by Huber include a thioamide substituent at the 3-position of the pyrazole ring, they

must be substituted at the 5-position of the ring by a hydroxy group or by other oxygen-linked groups such as an ether (e.g. $R_{205}O$-), alkylcarbonyloxy ($R_{205}C(O)O$-), alkyloxycarbonyloxy ($R_{205}OC(O)O$-), and the like.

Huber does not describe or suggest the premixes recited in the claims because Huber relates to compositions that comprise different compounds. As discussed above, the art of biologically active compounds is unpredictable, and based on Huber one of skill in the art would have no expectation of success that the compounds recited in the claims with significantly different substituents at the 5-position of the pyrazole ring would be effective as non-emetic formulations in premix compositions. One would only be guided to oral formulations that comprise arylpyrazole compounds that are substituted with a hydroxy or other oxygen-linked group at the 5-position of the pyrazole ring based on Huber. Based on the teaching of the broad genus formulae of Huber and Alig, which represent an enormous possible number of compounds and do not encompass the compounds recited in the claims, one of skill in the art would not be able to arrive at the compounds and premix compositions recited in the claims without the impermissible aid of hindsight.

Freehauf relates to stabilized formulations of ivermectin feed premix that exhibit an extended shelf life. The formulations of Freehauf include only an avermectin or milbemycin and optionally an insect growth regulator (IGR) active agent together with a pharmaceutically acceptable surfactant, a pharmaceutically acceptable wax, a pharmaceutically acceptable antioxidant and a pharmaceutically acceptable carrier. Freehauf does not describe or suggest feed premixes that contain any arylpyrazole active agents, much less the thioamide-substituted arylpyrazole compounds recited in the claims. Furthermore, Freehauf provides no motivation for one of skill in the art to use an arylpyrazole compound with the feed premix described.

None of Alig, Cleverly, Huber and Freehauf alone or in combination teach or suggest the premix recited in the claims. As discussed above, the arylpyrazole compounds recited in the claims are not taught or suggested by Alig or Huber, and the references provide no motivation to modify the compounds to attain the thioamide derivatives. Cleverly teaches chewable compositions that comprise various different active agents, but does not teach or suggest compositions containing thioamide arylpyrazole derivatives. Freehauf teaches a feed premix that comprises an avermectin or milbemycin active agent but does not teach or suggest a premix with an arylpyrazole active agent, much less a thioamide arylpyrazole derivative. Furthermore, the

combined teachings of the references do not provide any suggestion or motivation to attain any composition comprising the thioamide arylpyrazole derivatives, much less the premix compositions recited in the claims. Accordingly, Applicants respectfully submit that the claims are not obvious over the combined teaching of Alig, Cleverly, Huber and Freehauf. Withdrawal of the rejection is respectfully requested.

DOUBLE PATENTING REJECTION

Claims 26-29 and 33 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 4, 5, 8-10, 13, 15-21, 23-29 and 33 of co-pending Patent Application No. 11/580,731. Applicants note that this is a provisional double patenting rejection since the 11/580,731 application has not issued as a patent. Accordingly, Applicants reserve comments at this time.

CONCLUSION

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein, and issuance of a Notice of Allowance is respectfully requested.

If the Examiner believes any informalities remain in the application, which may be corrected by Examiner's amendment, or whether any other issues can be resolved by telephone interview, a telephone call with the undersigned attorney is courteously solicited.

The Commissioner is authorized to charge any additional fees, should they be due, to Deposit Account No. 50-2354.

Respectfully submitted,
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